REMARKS

Pending claims

Please note that claims 2-9, 11-28, and 45-50 were canceled by Applicants in paragraph 3 of the "Request for Filing a Patent Application Under 37 CFR 1.53(b)" filed with the application on June 28, 2001. Thus, claims 1, 10, 29-44 and 51-52 are currently pending.

Restriction Requirement

Applicants hereby elect, with traverse, to prosecute Groups X-XII, which includes and is drawn to Claims 10, 30-31, 33, 35-42, and 51-52. As the subject matter of new claim 53 corresponds to that of claims 51 and 52, it has been included by Applicants in this Group. Applicants reserve the right to prosecute the subject matter of non-elected claims in subsequent divisional applications.

Applicants traverse the Restriction Requirement for at least the following reasons.

The prior art searches for the claims of Groups I-III and IV-VI would substantially overlap

Groups I-III and Groups X-XII are allegedly distinct from those of Groups X-XII because they are allegedly "structurally and functionally different products, which are made by different methods and have different uses." See page 3 of the Restriction Requirement currently under consideration.

Applicants disagree with the Examiner's reasoning. The claims of Groups I-III and those of Groups IV-VI share a common technical feature in that the antibodies of Groups IV-VI, respectively, specifically bind the polypeptides of Groups I-III, respectively. Hence, a search of the literature with respect to the claimed polypeptides will necessarily yield references which disclose antibodies specific for those polypeptides, and vice versa. Therefore, both inventions could be examined at the same time without any additional burden on the Examiner. Therefore, Applicants respectfully request that the Restriction Requirement be withdrawn as between Groups I-III and Groups IV-VI.

The subject Matter of the Group I-III claims were already searched in an ancestor application

Applicants further traverse on the grounds that the Examiner could examine the claims of Groups I-III simultaneously with those of Groups IV-VI, again without undue burden, in view of the fact that they are related to, although of different scope from, claims already allowed in an ancestor application. For the Examiner's convenience, those claims are as follows:

U. S. Patent No. 6,281,334:

1. A purified polypeptide comprising an amino acid sequence selected from the group consisting of:

a) SEQ ID NO:3, SEQ ID NO:5, and

b) a fragment of SEQ ID NO:3 consisting of at least fifteen contiguous amino acid residues from about amino acid residue A309 to about amino acid residue G440 of SEQ ID NO:3.

2. A purified protein associated with apoptosis having at least 90% amino acid identity over the complete sequence of the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5, and which possesses apoptosis activity.

3. A composition comprising the polypeptide of claim 1 in conjunction with a suitable pharmaceutical carrier.

4. A method for using a protein to screen a plurality of other molecules or compounds for a molecule or compound which specifically binds the protein, the method comprising:

(a) combining the protein of claim 1 with the molecules or compounds under conditions suitable to allow complex formation, and

(b) detecting complex formation, wherein the presence of the complex identifies a molecule or compound which specifically binds the protein.

5. The method of claim 4, wherein the molecule or compound is selected from the group consisting of inhibitors, peptides, antibodies, immunoglogulins, and pharmaceutical agents.

6. A method for screening a compound for effectiveness as an agonist of a polypeptide of claim 1, possessing apoptotic activity the method comprising:

a) exposing a sample comprising a polypeptide of claim 1 to a compound, and

b) detecting an agonist of apoptotic activity in the sample.

7. A method for screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, possessing apoptotic activity the method comprising:

a) exposing a sample comprising a polypeptide of claim 1 to a compound, and

b) detecting an antagonist apoptotic activity in the sample.

8. A method of using a protein or a fragment thereof to purify a molecule or compound which specifically binds the protein from a sample, the method comprising:

a) combining the protein or a fragment thereof of claim 1 with a sample under conditions to allow specific binding;

b) recovering the bound protein; and

d) separating the protein from the molecule or compound, thereby obtaining purified molecule or compound.

Claim 1 of the instant application is related to claims 1 and 2 of U.S. Patent No. 6, 281,334 (hereinafter "the '334 patent"), although of broader scope. Applicants respectfully point out that, in light of the fact that claims 1 and 2 of the '334 patent have already been searched, examination of claim 1 of the instant application would result in minimal additional search burden to the Examiner.

Applicants additionally submit that in any case, the additional burden on the Examiner to examine the claims of Groups I-III in addition to the claims of Groups IV-VI, when balanced against the additional burden on Applicants to file, prosecute and maintain yet additional applications in this family. They therefore respectfully request that the Examiner consider Examining the claims of Groups I-III together with those of Groups IV-VI.

Accordingly, because the search required to identify prior art relevant to the claims of Groups I-III and IV-VI would substantially overlap, and because the subject matter of Groups I-III has previously been searched pursuant to allowance of related claims in an ancestor application, Applicants respectfully submit that simultaneous examination of the claims of those Groups would pose no undue burden. Thus, Applicants request reconsideration and withdrawal of the Restriction Requirement and examination of the claims of Groups I-VI.

The Election of Species Requirement: Requirements for "Markush Group" Practice

By dividing each grouping of claims into three separate Invention Groups, the Examiner is effectively requiring an Election of Species as between elements in a Markush group, those elements being SEQ ID NOs:1, 3 and 5 with respect to the polypeptides recited in claim 1, and the antibody species which specifically bind to each of those polypeptides recited in the remaining claims. **Pursuant to the requirement at paragraph 5 on page 4 of the Restriction Requirement under reply, Applicants provisionally elect Group III, which includes claim 1 as it relates to SEQ ID NO:5;**

however, Applicants traverse the "restriction requirement" in this regard as being improper in light of the PTO's own requirements for Markush practice.

§ 803.02:of the 8th Edition of the M.P.E.P. (August 2001) provides:

PRACTICE RE MARKUSH-TYPE CLAIMS

If the members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas,* 580 F.2d 461, 198 USPQ 334 (CCPA 1978), **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, **unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.**

This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from

> further consideration. As in the prevailing practice, a second action on the rejected claims would be made final.
>
> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a *non-elected species,* the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry. [emphasis added]

As can be seen from the above, it is clear that the present Restriction Requirement does not meet the Patent Office's own requirements.

The Examiner asserts that each of the polypeptides, and the antibodies specific for each of those polypeptides, which Applicants consider to be their invention, are distinct because they are "structurally and functionally different products, which are made by different methods and have different uses." Page 5, lines 4-5 of the Restriction Requirement.

However, is noted that if the number of "members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to **independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.**" Withdrawal of the restriction requirement, at least as between a reasonable number of the specific sequences each in the claims is required on that basis alone.

Furthermore, **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. The polypeptides and antibodies of the present invention, share a common utility in, for example, toxicology studies based on expression profiling; diagnostic assays for APOP, including methods for diagnosing

disease associated with over- or under-expression of APOP; drug screening techniques; purification of APOP (in the case of the claimed antibodies); .

In addition, Applicants respectfully submit that the polypeptides of SEQ ID NOs:1, 3 and 5 share common utility as they share homology to proteins associated with cell proliferation. This homology, and the common utility derived from this homology, are disclosed in the Specification. See, e.g, Applicants' Specification at pages 15, line 13 to page 17, line 30; page 27, line 30 to page 28 line 8; page 33, line 2 to page 34, line 25; page 41, lines 1-14; page 48, lines 5-24, and Figures 2A-B, 5A-B, and 8A-B. Hence the polypeptides of the invention do indeed share a "structural feature." Furthermore, even if the claims could be considered to be "Markush-type generic claims which include a plurality of alternatively usable substances or members," it is further noted that the M.P.E.P states that "A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits." This clearly applies in the present case.

Finally, Examiner's attention is directed to the M.P.E.P. at § 803.04 (Restriction - Nucleotide Sequences, EXAMPLES OF NUCLEOTIDE SEQUENCE CLAIMS) which states:

> Applications claiming more than ten individual independent and distinct nucleotide sequences in alternative form, such as set forth in example (A), will be subject to a restriction requirement. Only the ten nucleotide sequences selected in response to the restriction requirement and any other claimed sequences which are patentably indistinct therefrom will be examined.
>
> Applications claiming only a combination of nucleotide sequences, such as set forth in example (B), will generally not be subject to a restriction requirement. The presence of one novel and nonobvious sequence within the combination will render the entire combination allowable. The combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the examiner to maximize the identification of an allowable sequence. If no individual nucleotide sequence is found to be allowable, the examiner will consider whether the combination of sequences taken as a whole renders the claim allowable.

The instant application claims 3 polypeptide sequences (SEQ ID NOs:1, 3 and 5), as well as antibodies specific for those polypeptides. Hence, the claims examined clearly should not be limited by an election of only a single sequence under the guidelines set forth in the M.P.E.P. at § 803.04.

Therefore, it is respectfully submitted that, upon searching and examining SEQ ID NOs:1, 3 and 5, and finding no prior art over which SEQ ID NOs:1, 3 and 5 can be rejected, the Examiner must extend the search of the Markush-type claim to include the non-elected species.

3. "Rejoinder"

Finally, Applicants submit that claims 29, 43-44 of Groups VII-IX, as well as claims 32 and 34 of Groups X-XII, are methods of using the antibodies of Groups IV-VI, which should be examined together with the antibodies of Group IV-VI, per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products.

Applicants reserve the right to prosecute the subject matter of non-elected claims, or of any subject matter disclosed but not herein claimed, in a later continuation or divisional application.

It is noted that, while Applicants have canceled and not repeated new versions of claims 2-9, 11-28, and 45-49, Applicants expressly assert that these claims have been canceled for reasons relating to cost and efficiency of prosecution of the presently elected claims, and not for reasons relating to patentability. Applicants further expressly reserve the right to pursue the subject matter of those canceled claims, or any other subject matter disclosed but not herein claimed, in a later continuation or divisional application.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: 12/17/02

Cathleen M Rocco

Cathleen M. Rocco
Reg. No. 46,172
Direct Dial Telephone: (650) 845-4587

3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph claiming benefit of priority under 35 U.S.C. § 120 to prior-filed U.S. applications, beginning at the top of page 1, has been amended as follows:

"This application is a divisional application of U.S. application Serial Number 09/410,372 filed on September 30, 1999, [which is] and issued on August 28, 2001, as U.S. Patent Number 6,281,334, entitled PROTEINS ASSOCIATED WITH CELL PROLIFERATION. That application is in turn a divisional application of U.S. application Serial Number 08/958,335 filed on December 4, 1997, and issued on June 27, 2000, as U.S. Patent Number 6,080,847, entitled PROTEINS ASSOCIATED WITH CELL PROLIFERATION[,the contents all of which]. The contents of all of the foregoing patent applications and issued patents are hereby incorporated by reference.